PACKAGE LEAFLET

Package leaflet: Information for the patient

Grafalon 20 mg/ml concentrate for solution for infusion
anti-human T-lymphocyte immunoglobulin from rabbits

Read all of this leaflet carefully
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Grafalon is and what it is used for

Grafalon belongs to a group of medicines called immunosuppressants. Immunosuppressants are used to prevent the body from rejecting a transplanted organ.

You may be given Grafalon if you have had or are going to have an **organ transplant**. This is to prevent your body's immune system from rejecting a new organ. Grafalon helps to prevent or to stop this rejection response by blocking the development of special cells, which would normally attack the transplanted organ.

Grafalon is used as part of **immunosuppressive therapy**, together with other immunosuppressive medicines.

2. What you need to know before Grafalon is given to you

Do not have Grafalon at all and tell your doctor …
- if you are **allergic** to anti-human T-lymphocyte immunoglobulin from rabbits or any of the other ingredients of this medicine (listed in section 6)
- if you are suffering from an **infection**, where treatment is not working;
- if you have difficulty stopping **bleeding**;
- if you have a **tumor**.

Warnings and precautions

It is important to tell your doctor if you suffer from the following. You may be able to have Grafalon, but need to discuss with your doctor first.
- If you have previously had **allergic reactions** to these medicines (immunosuppressants) or rabbit proteins
- If you have **liver disease**
- If you have **heart problems**

Infections with Grafalon
Grafalon lowers your body's own defense system. As a result, your body will not be as good as it normally is at fighting **infections**. Your doctor will treat these infections appropriately.

Other medicines and Grafalon
Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. **These medicines may interfere with the effect of Grafalon.**

- Grafalon is used together with other immunosuppressive medicines, such as **corticosteroids**. Taking Grafalon at the same time as these other immunosuppressants may increase the risk of infection, abnormal bleeding and anemia (a blood disorder).

- **Live vaccines** may not be given to you because of your immunosuppressive treatment. If you are given a **non-live vaccine**, please tell your doctor. These vaccines may not work as well if taken at the same time as Grafalon.

Grafalon and older people (patients aged 65 years and over)
Grafalon can be given to older people. But not many older people have used it up to now. Your doctor may discuss this with you before you are given Grafalon.

Grafalon in children and adolescents (aged 2 to 17 years)
Grafalon can be given to children and adolescents. But not many children and adolescents have used it up to now. Your doctor may discuss this with you before you are given Grafalon.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. If it is necessary for you to take Grafalon, your doctor will discuss the risks and benefits of taking it during pregnancy. Grafalon can pass into breast milk.

Important information on the manufacture of Grafalon

Human components (e.g. red blood cells) are used in the production of Grafalon. Therefore certain measures are put in place to prevent infective agents being passed on to patients. These include careful selection of donors to make sure that those at risk of carrying infections are excluded, and the testing of each donation for signs of virus/infections. The manufacturing process also includes steps in the processing of human components that can inactivate or remove viruses. Despite these measures, when medicines for which human components are used in the production are administered, the possibility of passing on infections cannot be totally excluded. This can also apply to any unknown or emerging viruses or other types of infections.

The measures taken for Grafalon are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus, and for the non-enveloped hepatitis A and parvovirus B19 viruses.

Important information about excipients of Grafalon
Grafalon contains sodium, but less than 1 mmol (23 mg) sodium per dosing unit, i.e. it is nearly "sodium-free". The sodium content of the ready-to-use infusion solution is higher and depends on the amount of sodium chloride solution used for the dilution.

3. How to use Grafalon
Your treatment with Grafalon has been prescribed by a qualified doctor experienced in immunosuppressive treatment.

You will be given Grafalon in hospital. Grafalon will be given by infusion into a vein. Before the infusion is given to you it will be diluted in sodium chloride solution.

Adults and children can be given one of the following doses, based on their weight and condition:

If you are **going to have** an organ transplant
The usual daily dose is 2-5 mg/kg body weight. Treatment lasts 5 to 14 days

If you **have had** an organ transplant
The usual daily dose will be 3-5 mg/kg body weight. Your course of treatment will last 5 to 14 days.

Use in children and adolescents

Available information indicates that paediatric patients do not require a different dosage than adult patients.

If you are wrongly given too much Grafalon

Grafalon will be stopped and other immunosuppressive treatment will be altered. Your immune system might be weakened following too much Grafalon, so medicines to stop infections from developing may be given.

If you have any further questions on the use of this medicine ask your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor immediately if you notice any side-effects of allergic reactions and anaphylactic shock listed below:

Allergic reactions are common side-effects, following treatment with Grafalon. Less than 1 in 10 patients are likely to suffer:
- chest pain
- wheezing
- muscle pain
- reddening of the skin

In 3 out of more than 240 patients allergic reactions developed into **anaphylactic shock**. This is a serious and potentially life-threatening condition where the patient may present the following symptoms:
- high fever
- skin rash
- swelling
- breathing difficulties
- low blood pressure

Tell your doctor if you notice any side-effects listed below:

Very common side-effects likely to affect more than 1 in every 10 patients:
- fever
- chills
- headache
- tremor
- vomiting
- nausea
- diarrhea
- abdominal pain
- breathing difficulties
- flushing
- increased rate of infections
- low count of red blood cells (anemia)

Common side-effects likely to affect less than 1 in every 10 patients:
- thrombocytopenia, leukopenia, pancytopenia (blood disorders)
- inflammation of mucosa
- swelling
- feeling tired
- chest pain
- joint and muscle pain
- back pain
- muscle stiffness
- low or high blood pressure
- sensation of tingling, pricking, or numbness in the skin
- fast beating of heart
- light sensitivity
- elevation of laboratory parameters
- increased bilirubin in the blood
- blood in urine
- cough
- nose bleeding
- reddening of skin
- itching
- rash
- kidney tubular necrosis (kidney function failure)
- lymphoproliferative disorder (type of cancer that originates from certain white blood cells)
- venoocclusive disease (blocked small veins in the liver)

Uncommon side-effects likely to affect less than 1 in every 100 patients:
- indigestion
- mucosal inflammation caused by reflux of gastric secrete into the esophagus
- elevation of liver laboratory parameters
- elevation of cholesterol
- shock
- increased numbers of red blood cells
- abnormal collection of lymph
- water retention

Rare but medically important side-effects likely to affect less than 1 in every 1 000 patients:
- Hemolysis (abnormal breakdown of red blood cells)

In rare cases, especially if the drug is given over prolonged period of time, serum sickness could develop, which is a type of allergic reaction to foreign protein and is represented by such symptoms like fever, muscle and joint pain and itchy skin rash.

Additional side effects in children and adolescents
Available information indicates that the side effects of Grafalon in children and adolescents are not fundamentally different to the side effects seen in adults.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Grafalon

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the label after the EXP. The expiry date refers to the last day of that month.
- Grafalon should be stored in a refrigerator (2 °C - 8 °C) with the unopened vial kept in the outer carton to protect it from light.
- Do not use this medicine if the solution is cloudy.
- Any unused medicines will be disposed of by your doctor.
- Siliconized syringes must not be used for the withdrawal of Grafalon from the vials or for the production of the infusion solution.
- Not intended for multiple withdrawals.

6. Contents of the pack and other information

What Grafalon contains

The **active substance** is 20 mg/ml anti-human T-lymphocyte immunoglobulin from rabbits.
The other ingredients are sodium dihydrogen phosphate dihydrate, phosphoric acid (85%) and water for injections.

What Grafalon looks like and contents of the pack

Grafalon is a clear to slightly opalescent and colourless to pale yellow solution in glass vials. The smaller 5 ml size vial contains 100 mg of Grafalon, whilst the larger 10 ml size vial contains 200 mg of Grafalon.

Grafalon comes in a box containing either 1 vial or 10 vials.

The Marketing Authorisation Holder and Manufacturer is

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Germany

This leaflet was last revised in December 2024.